

## REMARKS

Favorable reconsideration by the Examiner in view of the herewith presented amendment and remarks is respectfully requested.

The present claims refer to a method for treatment of a necrosis or wound and a main feature of the instant invention is the reversibility of the gel which is composed of aliphatic chains attached to polysaccharide macromolecules.

Reversibility has as an advantage the possibility of applying the treatment product to a wound in a liquid state so that it spreads over the wound, conforms to the shape of the wound, sets to a gel and can liquefy again when it is close to the wound because of body heat or ionic strength.

This feature is an important one and these elements are recited in new claim 17 which is a combination of old claims 17 and 18.

Reversibility depends on the nature of the cross links between macromolecules. In the present invention one forms physical gels. A description of this kind of gel is given in the attached article "Biodegradable hydrogels for drug delivery" pages 99 and 100. The gels are caused by multiple weak junction zones between the aliphatic chains of different macromolecules, see line 4 at page 5 of the present specification referring to hydrophobic interactions between the associated arms. (Also mentioned in "Macromolecular complexes... " and the article "Amphiphilic derivatives of sodium alginate.... " hereto attached).

These bonds differ from the strong chemical gels. Moreover there is a relationship between reversibility and substitution rate, i.e., extent of esterification. In the examples of the specification at pages 7, a level of substitution of the order of 8% is given.

Another feature of the invention are the highly effective intrinsic natural curative properties of the system to be found in the aliphatic chains. Additional molecules of an active principle may be trapped inside the alveoli but it is not compulsory for obtaining the curative effect.

Claims have been rejected under 35 USC § 103 as allegedly being unpatentable over Francesco et al combined with WO 9637519.

Applicant respectfully traverses this rejection.

Francesco discloses the general medical, surgical, cosmetic and food use of esters of alginic acid (abstract). This citation covers a very large scope of products and uses but there is no information relating to the present invention.

The Examiner refers to the ophthalmological application, col. 16. It is to be noted that Francesco only discloses that an amorphous powder on contact of the tissue constitutes a concentrated aqueous solution of a gelatinous character with viscous consistency and elastic properties. There is no indication of reversibility. There is a passage from an anhydrous solid state to a gel state. Francesco does not teach the use of a reversible gel. In fact a reversible gel would not be suitable because it would liquefy and would make vision indistinct.

Therefore, Francesco teaches the use of irreversible gels.

This is confirmed at col. 12 lines 58-62: *"for the manufacture of sanitary surgical articles it is preferable to use total or partial esters with a high grade of esterification, for example between 80% and 100% of all the carboxy groups present."* The citation refers at lines 63-68 to a wide interval between 5% and 90% but is for a very broad group of purposes comprising alimentary, cosmetic and pharmaceutical. One can conclude that for the ophthalmological use the reference intends a gel with at least 80% esterification grade that is certainly not reversible.

It should be pointed out that the WO citation refers to chemical gels. At page 3 lines 20-24: *"the new compounds present a compact, three dimensional structure (wall to wall) the latter are therefore characterized by greater mechanical resistance"*.

This new compound is to be opposed to *"the gels constituted by inner esters of haluronic bound together by simple, physical-type bonds"* (page 3, lines 18-20).

The gels of the present invention should be placed in the second category. They have a weak bond. Because of the weak nature of the bond they are reversible.

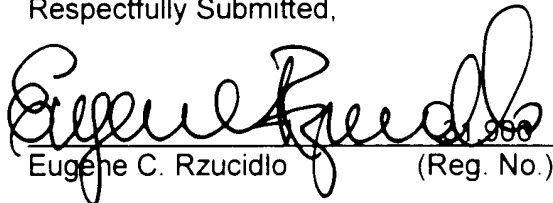
On the contrary such a feature does not belong to the gels of WO that are reversible. The process includes the step of *"subjecting the article to radiation selected from the group consisting of UV, beta or gamma radiation"* page 7 lines 5-6. The applications as film membranes, fibers or threads (page 6) are clearly not the kind of use that is claimed where the product is poured in a liquid state into the wound or necrosis.

It is urged that the cited references do not teach the use of a product that is first in a solution state then in a gel state and that will liquefy again proximate to the tissue of the wound under external strains such as body heat or ionic strength.

For the above, reasons, Applicant urges that the Examiner's rejection is in error and reconsideration and withdrawal thereof is urged to be proper. If the Examiner believes that issues may be resolved by a telephone interview, the Examiner is respectfully urged to telephone the undersigned at (212) 801-2100. The undersigned may also be contacted by e-mail at [ecr@gtlaw.com](mailto:ecr@gtlaw.com). Please charge all required fees to the Greenberg Traurig LLP Deposit Account No. 50-1561.

Respectfully Submitted,

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## ATTACHMENT A

17. A method for treatment of a necrosis or wound comprising:

preparing a wound-treatment product, adapted to change state in a reversible manner from a solution state to a gel state and from a gel state to a solution state, the product comprising aliphatic chains attached to polysaccharide macromolecules, wherein each aliphatic chain is attached to a single polysaccharide macromolecule; wound;

changing the state of at least a portion of the product from the solution state to the gel state;

and liquefying that portion of the product proximate to the wound or necrosis by at least one of application of an external force, body heat, or ionic strength.